

period of 6 weeks. After 2 months she developed malaise and persistent fever (38–38.5°C) without clinical or laboratory evidence of infection or hemolysis. Interferon- $\alpha$ -2b was ceased with resolution of fever, and she subsequently remains well on hydroxyurea.

A causal association between interferon- $\alpha$ -2a and intravascular hemolysis is suggested by the close temporal relationship of onset of symptoms with the first dose of the drug, the rapid resolution with its withdrawal, and the exclusion of other known causes of intravascular hemolysis. The mechanism by which interferon caused the hemolysis is unclear. Autoimmune hemolysis has been associated with interferon use, but is usually a long-term complication, occurring after a median of 14 months of treatment [1]. In our patient, hemolysis was not obviously immune-mediated, in view of the time course and the inability to detect either IgG or C3 on the red-cell surface. Furthermore, it is difficult to explain hemolysis with interferon- $\alpha$ -2a, but not  $\alpha$ -2b, on an immunogenic basis when the biochemical difference between the two is confined to a single amino acid at position 22 [2].

Interferon- $\alpha$ -2a is cloned in an *Escherichia coli* strain, with a final purity >99% [3,4]. While it is theoretically possible that our patient reacted to a "contaminating" *E. coli* protein, we are not aware of reports of intravascular hemolysis associated with biological substances cloned in this way [5].

In the absence of other demonstrable causes, it is likely that the hemolysis was interferon-induced. Nonimmune intravascular hemolysis should be added to the list of potential complications of this drug.

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#### Acrocyanosis as a Herald Sign of Ovarian Benign Teratoma

*To the Editor:* We report on the uncommon association of cryoagglutinins without hemolysis, which subsided following surgical ablation of an ovarian benign teratoma.

#### CASE REPORT

A 22-year-old woman was admitted at our Institution for persistent acrocyanosis. Previous vascular (Doppler and capillaroscopy) investigations and present physical findings were unremarkable. Chest X-rays, bone-marrow biopsy, thyroid hormones, erythrocyte sedimentation rate (ESR), C-reactive protein, rheuma test, antinuclear antibody (ANA), immunoglobulin serum levels, lactate dehydrogenase (LDH), aptoglobin, Coombs' test, beta2 microglobulins, serum copper, and serum markers of viral infection were all normal or negative. Cryoagglutinins were 1:2,000. Computed tomography scanning showed the presence of a dermoid cyst 9 × 5 cm, close to her

left ovary. Following surgical ablation of this tumor (the pathological diagnosis being of ovarian benign teratoma), cryoagglutinins and acrocyanosis disappeared. The patient is well 18 months after surgery.

#### DISCUSSION

The association of autoimmune hemolytic anemia and benign ovarian neoplasm is uncommon in adult patients [1,2]. Our case is exceptional in that the patient, although she had high-titer cryoagglutinins, never became anemic, and there was no evidence of hemolysis.

In our Medline-assisted literature search (for 1987–1995) we were unable to find any similar cases, and we believe ours to be the first report of acrocyanosis heralding an ovarian benign teratoma. We also tend to believe that the resolution of acrocyanosis and the disappearance of cryoagglutinins following surgery rule out a chance association among the three. Indeed, cryoagglutinins and acrocyanosis are known to be causally linked [3], and the development of autoimmune hemolytic anemia is a well-known paraneoplastic sign [4] in a variety of cancers (lymphomas, lung, ovary, tumors of the gastrointestinal tract, etc.). The absence of hemolymphopoietic tissue in the pathological specimen fits with the hypothesis that benign teratoma is not a site of direct cryoagglutinin production but that it serves as a stimulus for such production to occur in normal lymphoid tissue of the host. Once such stimulus was surgically removed, the cryoagglutinins disappeared. Our observation is worth further confirmation: owing to their subclinical manifestation, it is quite conceivable that cryoagglutinin production may have been overlooked in previous cases of teratomas. Accordingly, we propose that cryoagglutinins be systematically sought in benign ovarian teratomas to ascertain the hypothesis that their prevalence is increased in such patients as compared to a control population.

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#### Aplastic Anemia During Treatment With Albendazole

*To the Editor:* Albendazole is a benzimidazole-carbamate compound whose use is rising in the medical treatment of hydatid disease [1]. Adverse